HANTAVIRUS

Also known as Hantavirus Pulmonary Syndrome (HPS) and Sin Nombre

✓DISEASE AND EPIDEMIOLOGY

Clinical Description:

Hantavirus Pulmonary Syndrome (HPS) is an acute febrile illness that progresses rapidly to severe respiratory compromise that usually requires supplemental oxygen and clinically resembles (adult respiratory distress syndrome [ARDS]). Symptoms may develop between 1 and 5 weeks after exposure to fresh urine, droppings, or saliva of infected rodents. Clinical findings during the 3–5 day prodrome are nonspecific, flu-like symptoms, including fever, fatigue, and muscle aches—especially in the large muscle groups. Gastrointestinal manifestations and dizziness may accompany these symptoms. As the disease progresses, symptoms can include cough and shortness of breath as the lungs fill with fluid. Once the cardiopulmonary phase begins, the disease progresses rapidly, necessitating hospitalization, and often, assisted ventilation within 24 hours. Renal failure and hemorrhagic manifestations, while common in Hemorrhagic Fever with Renal Syndrome (HFRS), have been mild or absent in most recognized cases of HPS. In survivors, recovery from the acute illness is rapid, with apparent restoration of normal lung function. HFRS includes hypotension, kidney failure, and bleeding.

Causative Agent:

Hantaviruses are single-stranded RNA viruses belonging to the bunyavirus family. Numerous hantavirus species exist. They are responsible for two primary syndromes: hantavirus pulmonary syndrome (HPS) and hemorrhagic fever with renal syndrome (HFRS).

Differential Diagnosis:

Differential diagnoses include: pneumococcal sepsis, viral myocarditis, atypical pneumonia, leptospirosis, Legionnaire's disease, mycoplasma, Q fever, Chlamydia, opportunistic infection, and in regions where the organisms are present, septicemic plague, tularemia, coccidioidomycosis and histoplamosis. Non-infectious conditions such as Goodpasture's syndrome should also be considered.

Laboratory identification:

A positive serological test result, evidence of viral antigen in tissue by immunohistochemistry, or the presence of amplifiable viral RNA sequences in blood or tissue, with compatible history of HPS, is considered diagnostic for HPS.

> **USL:PH:** The USL:PH is available to confirm positive or inconclusive serologies from clinical laboratories. The USL:PH may be able to provide primary testing for hantavirus under certain circumstances. Please contact USL:PH at (801)965-2400 for more information.

Treatment:

There is no specific treatment or cure for hantavirus infection. Treatment of patients with HPS remains supportive in nature. Patients should receive appropriate, broad-spectrum antibiotic therapy while awaiting confirmation of a diagnosis of HPS. Care during the initial stages of the disease should include antipyretics and analgesia as needed.

If there is a high degree of suspicion of HPS, patients should be immediately transferred to an emergency department or intensive care unit (ICU) for close monitoring and care. Patients presenting with fulminant illness due to HPS have a poor prognosis despite ICU care. ICU management should include careful assessment, monitoring and adjustment of volume status and cardiac function, including inotropic and vasopressor support if needed. Fluids should be administered carefully due to the potential for capillary leakage. Supplemental oxygen should be administered if patients become hypoxic. Equipment and materials for intubation and mechanical ventilation should be readily available since onset of respiratory failure may be precipitous.

Intravenous ribavirin, a guanosine analogue, has not been shown to be effective for treatment of HPS despite its effects on a related disease, hemorrhagic fever with renal syndrome (HFRS), which is caused by Old World hantaviruses. Controlled trials showed a reduction in case-fatality for HFRS patients treated with ribavirin. However, despite in vitro activity of ribavirin against Sin Nombre Virus (SNV), neither an open-label trial conducted during the 1993 outbreak nor an attempted placebo-controlled trial demonstrated clinical benefit for HPS. Ribavirin is not recommended for treatment of HPS and is not available for this use under any existing research protocol.

Take-home Message for Care Providers
Rapid transfer to ICU
Careful monitoring
Fluid balance
Electrolyte balance
Blood pressure

Case fatality:

The mortality rate is still not well-defined, but it appears to be approximately 35–50%. Mortality rates for HFRS range from 5–15%.

Reservoir:

There are multiple hantaviruses species that cause HPS, and they are each associated primarily with a single rodent species. The main reservoir for SNV is the deer mouse, *Peromyscus maniculatus,* present throughout the western and central U.S. and Canada. Black Creek Canal virus is associated with the cotton rat, *Sigmodon hispidus*, found in the Southeast. The rice rat, *Oryzomys palustris*, found in the southern states of the U.S., acts as a reservoir for Bayou virus. In the northeastern states, the white-footed deer mouse, *Peromyscus leucopus,* has been associated with the New York-1 strain of hantavirus. The prevalence of infection in rodents varies greatly. Infected rodents generally develop a chronic, asymptomatic infection and can shed live virus in their

saliva, feces, and urine throughout their lives. The duration of viremia and the persistence of virus in tissues indicate that rodents can contaminate the environment through their excretions and secretions for long periods.

Transmission:

Rodents shed the virus in their urine and feces. Humans are infected when they inhale dust that contains dried contaminated rodent urine or feces. Transmission may also occur when dried materials contaminated by rodent feces or urine are disturbed and are directly introduced into broken skin or into the eyes, nose, or mouth. There is no evidence of person-to-person transmission of HPS in the U.S.

Susceptibility:

Persons without serological evidence of past infection appear to be uniformly susceptible. Inapparent infections occur; second attacks have not been documented, but the protection and duration of immunity conferred by previous infection is unknown.

Incubation period:

Since HPS is relatively uncommon, the incubation period has not yet been well-defined; it is believed to range from about 1–5 weeks, with an average of about 2 weeks.

Period of communicability:

There has been no evidence of person-to-person spread of hantavirus in the U.S. Rodents can develop a chronic, asymptomatic infection with hantavirus and can remain infectious throughout their lives.

Epidemiology:

HPS was first recognized in 1993; as of December 10, 2010, 560 cases have been confirmed in the U.S. Cases have been reported in 32 states, including most of the western half of the country and some eastern states as well. Over half of the confirmed cases have been reported from areas outside of the Four Corners area. About 75% of patients with HPS have been residents of rural areas. The distribution of identified cases reflects a seasonal trend, with peaks during the spring and the summer, although cases have occurred throughout the year. Any person whose occupation (e.g., biologist, pest-control worker) put him/her in frequent contact with rodents or their droppings is potentially at risk of getting the disease. Travel to and within all areas where hantavirus infection has been reported is not considered a risk factor for infection with HPS. The possibility of exposure to hantavirus for campers, hikers, and tourists is very small and is reduced further if steps are taken to reduce rodent contact. Disturbing or inhabiting closed, actively rodent-infested structures is an important risk factor for contracting HPS.

HPS occurs in North and South America. There are several hantaviruses associated with HPS in the U.S. SNV is the agent responsible for the 1993 HPS epidemic, which occurred in the southwestern U.S and remains the primary causative agent of HPS in the United States. Black Creek Canal virus was implicated in a single HPS case in Florida. Bayou virus was discovered in cases in Louisiana and Texas. New York-1 virus is similar

to SNV, but it is distinct enough to suggest that it is a variant found in the eastern third of the U.S. Most cases of HPS have been associated with SNV. HFRS caused by Hantaan virus or by Dobrava-Belgrade virus occurs mainly in rural areas of Asia and the Balkans. Seoul virus, which has a worldwide distribution, causes HFRS of variable severity. The Puumala virus causes milder HFRS in Europe. However, person-to-person transmission, including nosocomial transmission of Andes virus, was well documented for a single outbreak in southern Argentina.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Identify the source of exposure and prevent further transmission.
- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.

Prevention: "Seal up, Trap up, Clean up!"

Environmental Measures

The best way to prevent hantavirus infection is to eliminate or minimize human contact with rodents or their excrement. Persons should:

- Clear brush, grass, and garbage from around building foundations to eliminate a source of nesting materials.
- Keep tight-fitting lids on all garbage cans.
- Use metal flashing around the base of wooden, earthen, or adobe dwellings to provide a strong metal barrier.
- Seal all entry holes ¼ inch wide or wider with lath screen or lath metal, cement, wire screening, or other patching materials, inside and out.
- Elevate hay, woodpiles, and garbage cans to eliminate possible nesting sites.
- Use an EPA-approved rodenticide with bait under plywood or plastic shelter along baseboards, or use trap, and properly dispose of rodents. Live trapping of rodents is not recommended.
- Clean all food preparation areas. Store all food (both human and pet) in rodent-proof containers.
- Do not leave open bowls of pet food outside. Discard any uneaten pet food properly at the end of the day.

Personal Preventive Measures/Education

People involved in cleaning rodent-contaminated areas should keep the following recommendations in mind:

- Clean droppings using a wet method, rather than a dry method such as sweeping or vacuuming. Spray disinfectant, such as dilute bleach, prior to cleaning, and use a wet mop or towels moistened with disinfectant to clean.
- Work in well-ventilated areas.

- Gloves, dust/mist masks, long-sleeved clothing, and protective eyewear may help prevent exposure.

Chemoprophylaxis:
None

Vaccine:
None

Isolation and quarantine requirements:
None

✓CASE INVESTIGATION

Reporting:
- Report all suspect and confirmed cases of hantavirus.

Hantavirus Pulmonary Syndrome (Hantavirus Disease) (HPS) 2010 Case Definition

Clinical description

Hantavirus pulmonary syndrome (HPS), commonly referred to as hantavirus disease, is a febrile illness characterized by bilateral interstitial pulmonary infiltrates and respiratory compromise usually requiring supplemental oxygen and clinically resembling acute respiratory disease syndrome (ARDS). The typical prodrome consists of fever, chills, myalgia, headache, and gastrointestinal symptoms. Typical clinical laboratory findings include hemoconcentration, left shift in the white blood cell count, neutrophilic leukocytosis, thrombocytopenia, and circulating immunoblasts.

Clinical case definition

An illness characterized by one or more of the following clinical features:

- A febrile illness (i.e., temperature greater than 101.0° F [greater than 38.3° C]) corroborated by bilateral diffuse interstitial edema or a clinical diagnosis of acute respiratory distress syndrome (ARDS) or radiographic evidence of noncardiogenic pulmonary edema, or unexplained respiratory illness resulting in death, and occurring in a previously healthy person.
- An unexplained respiratory illness resulting in death, with an autopsy examination demonstrating noncardiogenic pulmonary edema without an identifiable cause.

Laboratory criteria for diagnosis

- Detection of hantavirus-specific immunoglobulin M or rising titers of hantavirus-specific immunoglobulin G, or
- Detection of hantavirus-specific ribonucleic acid sequence by polymerase chain reaction in clinical specimens, or
- Detection of hantavirus antigen by immunohistochemistry

Case classification

- *Confirmed*: a clinically compatible case that is laboratory confirmed

Comment

Laboratory testing should be performed or confirmed at a reference laboratory. Because the clinical illness is nonspecific and ARDS is common, a screening case definition can be used to determine which patients to test. In general, a predisposing medical condition (e.g., chronic pulmonary disease, malignancy, trauma, burn, and surgery) is a more likely cause of ARDS than HPS, and patients who have these underlying conditions and ARDS need not be tested for hantavirus.

Case Investigation Process:

- Fill out morbidity form
- Verify case status.
- Fill out disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.
- The sample must be confirmed by USL:PH or the CDC in order to confirm the case.

Outbreaks:

More than one case of hantavirus with a common exposure constitutes an outbreak.

Identification of case contacts:

This disease is rarely spread person to person.

Case contact management:

Environmental assessment should be done to make sure that no one else will be exposed. Anyone else who was exposed to the environment that infected the case during the same time period, should be monitored for symptoms.

✓REFERENCES

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.l

Control of Communicable Diseases Manual (19th Edition), Heymann, D.L., Ed; 2008.

Red Book: 2009 Report of the Committee on Infectious Diseases (28th Edition), Larry K. Pickering MD, Ed; 2009.

Massachusetts Department of Health Hantavirus Disease Plan

"Seal Up! Trap Up! Clean Up! Protect Your Family from Hantavirus Pulmonary Syndrome (HPS)." Centers for Disease Control and Prevention. <www.cdc.gov/ncidod/diseases/hanta/hps_stc/stc_spot.htm>.

Centers for Disease Control and Prevention. Hantavirus. http://www.cdc.gov/hantavirus/